Deposited: January 8, 2007

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By: Julia L. Watts Date: January 8, 2007

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Claudia Cherney STEWART, et al.

Serial No.: 09/330,629

Filed: June 11, 1999

Art Unit: 1617

Examiner: San Ming R. Hui

Confirmation No.: 9658

Atty. Docket No.: JG-RP-4796/500561.20065

Customer No. 026418

METHOD OF HIV AND HPV PROPHYLAXIS

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

SUPPLEMENTAL RESPONSE TO OFFICE ACTION

Sir:

This Response is supplemental to the Response to the Office Action filed December 6, 2006.

Submitted herewith are several further references supporting Applicants' position that references relied on by the Examiner do not suggest that the presently claimed compounds could or should be used prophylactically.

It is well known that the viral life-cycle is complex and consists of a number of distinct stages, including cellular adhesion and viral entry, replication of viral nucleic

acid, synthesis of viral proteins, assembly and cellular exit of viral particles (see for example, Excerpt from Smith, et al. 2004, *Science*, 304:237 and Brock, et al., Biology of Microorganism, Sixth Ed. 1991, Prentice Hall, pgs. 189-190).

Each stage is a potential target for regulating the viral life-cycle by anti-viral agents, preventing certain stages in the viral life-cycle may continue generation of viral particles within a cell, i.e., a pre-existing viral infection, while preventing other stages may stop the initial step of viral infection of an unaffected cell, that is, preventing a viral infection.

For example, as evidence by Doms, et al., 2004 *New England Journal of Medicine*, 351:743-744, in particular, page 743, lines 1-15 of the article, a new class of agents to block the entry of a viral into the cell has recently been developed which may therefore have application in preventing viral infection, in addition to existing drugs that inhibit viral enzymes within the host cell and which therefore prevent post-infection replication of the virus.

Thus, it is not necessarily the case that a compound which is capable of treating an existing viral infection will also be capable of preventing a viral infection. For example, nucleoside analogs such as acyclovir and AZT, are capable of preventing viral replication but have no effect on viral entry.

As discussed in Crumpacker, in 2002 Fields Virology 4th Ed., 1(15):394-395, acyclovir is an analog of guanosine which enters a cell like other nucleotides. It is activated by a specific herpes virus enzyme, thymidine kinase, which is released inside the cell following penetration of the virus. The phosphorylated acyclovir molecules then inhibit viral DNA polymerase and stop viral DNA replication. Accordingly, acyclovir will have no effect on entry of the virus into a cell.

As discussed in Crumpacker, 2002 Fields Virology 4th Ed., 1(15):404-405, AZT is a drug widely used against HIV which Is a synthetic pyrimidine analogue that binds the great avidity to the reverse transcriptase of human immunodeficiency virus (HIV) when the virus is inside the cell and starts the phase of the replication of the viral nucleic acid. Since AZT can only act after it is phosphorylated inside the cell, it has no effect on extracellular virus particles or their mechanism of entry into a host cell.

Consequently, these references make it clear that one skilled in this art would not automatically assume that a compound which could be used for the treatment of a disease, i.e., the therapeutic treatment of a subject having the disease, could be used to prevent the viral infection and the very beginning, before it enters the cell.

Applicants submitted an article by Schwartz, et al., *Journal of Virology*, 75:4117-4128, with the last response. This article makes it clear that the compounds of the class claimed in the present application, i.e., CTC-96, exert their anti-viral effect by inhibiting entry of envelope viruses into host cells but have no effect on the accumulation of viral proteins after initiation of the infection (for example, page 4120 of Schwartz, et al.).

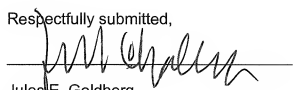
Accordingly, compounds of the invention can be used prophylactically, i.e., to prevent viral infection. However, while the mechanism of action of CTC-96 is now known, it was not known prior to the filing date of the present application, that it could be used prophylactically. Accordingly, it is submitted that claims as they presently stand, are patentable over the art of record and favorable reconsideration and Notice of Allowance are earnestly solicited.

An Information Disclosure Statement listing the references referred to above is enclosed along with copies of each of the references discussed.

It is also noted that forwarded herewith is a Notice of Appeal.

Respectfully submitted,

Dated: January 8, 2007



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